Brian Death

Perioperative Management of the Organ Donor

ASA VI

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Lecture Outline

- Historical development of death based on neurologic criteria.
- Diagnosis of brain death
- Pathophysiology of brain death
- Perioperative management of the organ donor

Evolution of the Criteria for Brain Death

Traditional concept of death

The cessation of life; the ceasing to exist; *defined by physicians* as a total stoppage of the circulation of the blood, and a cessation of the animal and vital functions consequent thereupon, such as respiration, pulsation, etc..

Black's Law Dictionary 4th Ed 1951

The traditional concept of death assumes the physician's determination

of death is based on the absence of all vital signs to include cardio-

pulmonary function without the consideration for the role of the brain.

Evolution of the Criteria for Brain Death

Common Law Statutes

Death is the total stoppage of the circulation of the blood and cessation of animal and vital functions consequent thereon, such as respiration, pulsation, etc..

Brain death: Legal issues Heart & Lung, Nov-Dec 1979, Vol. 8, No. 6

Common law definition of death persisted until the 1970's.

Multiple court rulings recognized the use of mechanical ventilation as supporting the cardiopulmonary system of a neurologically devistated individual and that that individual is dead.

Evolution of the Criteria for Brain Death

- 1950's Polio Epidemic

  Saw the first widespread use of mechanical ventilation.

- 1959 Mollaret and Goulon

  - Introduced the term *Coma depasse'* **irreversible coma**.

  - 23 comatose patients who had lost brainstem reflexes and spontaneous respiration.

  - Described the state of irreversible unconsciousness as verified by isoelectric EEG findings.

Evolution of the Criteria for Brain Death

- **1960's**

- Brought a refinement in surgical transplant techniques and immunosuppresive therapy.
- Death based on cessation of cardiopulmonary function remained necessary before organ procurement.
- The futility of supporting the vegetative functions of brain dead patients served as the impetus for develop-

  ment of standardized medical criteria and legal statutes for determining neurological death.

Evolution of the Criteria for Brain Death

- **1968 A Definition of Irreversible Coma**

  Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death

  JAMA, Aug 5, 1968 Vol 205, No. 6

  - Convened to define death based on neurologic criteria

  - Determine the **characteristics of irreversible coma**

  - Clarify and **standardize medical guidelines** for

    determining brain death.

Characteristics of Irreversible Coma

Unreceptivity and unresponsitivity A total unawareness to externally applied painful stimuli with complete unresponsiveness. Plantar or noxious stimulus gives no response.

Isoelectric elecroencephalogram

- Provides confirmatory data of cortical inactivity.
- At least 10 full minutes of recording is desirable.

Characteristics of Irreversible Coma

No reflexes Absence of elicitable brainstem reflexes

- Pupils fixed and dilated without response to light.
- Ocular movement and blinking are absent.
- No evidence of postural activity.
- Swallowing yawning vocalization are in abeyance.
- Absent corneal and pharyngeal reflexes.
- Plantar or noxious stimulation gives no response.

Characteristics of Irreversible Coma

No movements or Breathing No spontaneous muscular movement or spontaneous respiration for an observatory period of 1 hour. Total **absence of spontaneous breathing** may be established **if no respiratory effort is made for 3 minutes** with the ventilator off.

Exclusion of two conditions

- Hypothermia – core temp 90 F (32.2 C)
- CNS depressants (barbiturates, toxins)

2 separate examinations 24hrs apart

- Repeat clinical exam.
- No change establishes irreversibility of brain death.

Evolution for the Criteria for Brian Death

- **1970 National Institute of Neurological and Communicative Disorders and Stroke Collaboration Study.**

- Confirmed in prospective studies that patients who fulfilled the criteria of the Harvard committee did not recover neurologic function and that these constituted reliable criteria for brain death.

- 6 hours time interval between reexamination was confirmatory of irreversible coma.

Evolution of the Criteria for Brain Death

Statutory Brain Death 1974

"A person will be considered dead if in the announced opinion of a physician, based on ordinary standards of medical practice, he has experienced an irreversible cessation of spontaneous respiratory and circulatory functions. In the event that artificial means of support preclude a determination that these functions have ceased,

a person will be considered dead if in the announced opinion of a physician based on ordinary practice, he has experienced an irreversible cessation of spontaneous brain functions"

Brain death: legal issues, Heart and Lung 1979, Vol. 8, No. 6

Evolution of the Criteria for Brain Death

- **1974-1979** Approximately only half the states enacted legislative statues or judicial decisions recognizing death based on irreversible cessation of all functions of the brain.
- 1980 Model Brain Death Act

  "Guidelines for the Determination of Death"

Report of the Medical Consultants on the Diagnosis of Death to

the President's Commission for the Study of Ethical Problems in

Medicine and Biomedical and Behavioral Research

JAMA Nov 13, 1981 – Vol 246, No. 19

Evolution of the Criteria of Brian Death

The commission was tasked to:

- Propose a **model statute** for the determination of death intended for adoption in every jurisdiction.
- Suggest **uniform diagnostic criteria** for the determination of death based on current medical standards to include death based on neurologic criteria.

Representative consultants consisted of members from:

- American Bar Association, AMA, National Conference of Commissioners on Uniform Laws

Model Statute

Uniform Determination of Death Act

An individual who has sustained either (1) irreversible cessation of circulatory and respiratory function, or (2) irreversible cessation of all functions of the **entire brain**, including the **brain stem**, is dead. A determination of death must be made in accordance with accepted medical standards.

JAMA Nov 13, 1901 – Vol 246, No. 19

Uniform Criteria for the Determination of Death

Table 76–2. Criteria for Determination of Death

An individual representing the findings in either section A (cardiopulmonary) or section B (neurologic) is dead. In either section, a diagnosis of death requires that *both cessation of functions,* as set forth in subsection 1, and *irreversibility,* as set forth in subsection 2, be demonstrated.

A. An individual with irreversible cessation of circulatory and respiratory functions is dead.
   1. Cessation is recognized by an appropriate clinical examination.
   2. Irreversibility is recognized by persistent cessation of functions during an appropriate period of observation and/or trial of therapy.

B. An individual with irreversible cessation of all functions of the entire brain, including the brain stem, is dead.
   1. Cessation is recognized when evaluation discloses findings of a and b:
      a. Cerebral functions are absent,
         and
      b. Brain-stem functions are absent.
   2. Irreversibility is recognized when evaluation discloses findings of a and b and c:
      a. The cause of coma is established and is sufficient to account for the loss of brain functions,
         and
      b. the possibility of recovery of any brain functions is excluded,
         and
      c. the cessation of all brain functions persists for an appropriate period of observation and/or trial of therapy.

Complication Conditions
   A. Drug and metabolic intoxication.
   B. Hypothermia.
   C. Children.
   D. Shock.

From Medical Consultants on the Diagnosis of Death,[5] copyright 1981, American Medical Association

Modern Concept of Death

- Laws providing for the diagnosis of brain death currently exist in all 50 states.
- Any licensed medical physician can make the diagnosis
- Exceptions:

  - **California** requires that two licensed physicians make the diagnosis on the basis of a clinical examination and confirmatory test results.

  - **Virginia** requires a “specialist in the field of neurology, neurosurgery or EEG” to assist in making the determination.

Diagnosis of Brain Death Current practice guidelines

- **"Practice parameters for determining brain death in adults"**

  - Report of the Quality Standards Subcommittee of the American Academy of Neurology.

  - Outlines diagnostic criteria for the clinical diagnosis of brain death in patients older than 18 years.

  - Evidenced based review from 1976-1994.

NEUROLOGY 1995; 45: 1003-1014

- **Report of special task force: guidelines for the determination of brain death"**

  - American Academy of Pediatrics

PEDIATRICS 1987; 80: 298-300

Definition of Brain Death

- Definition:

Brian death is the total and *irreversible* loss of function of the *whole brain,* including *cerebral cortex* and *brain stem.*

Uniform Determination of Death Act

Report of the Medical Consultants on the Diagnosis of Death to the President's Commission for the Study of Ethical Problems in Medicine and Behavioral Research

JAMA Nov 13, 1981 – Vol 246, No. 19

Diagnosis of Brain Death

- Brain death is a clinical diagnosis. It can be made without confirmatory testing if you are able to establish the etiology, eliminate reversible causes of coma, complete fully the neurologic examination and apnea testing.
- The diagnosis requires demonstration of the absence of both cortical and brain stem activity, and demonstration of the irreversibility of this state.

Clinical Diagnosis of Brian Death

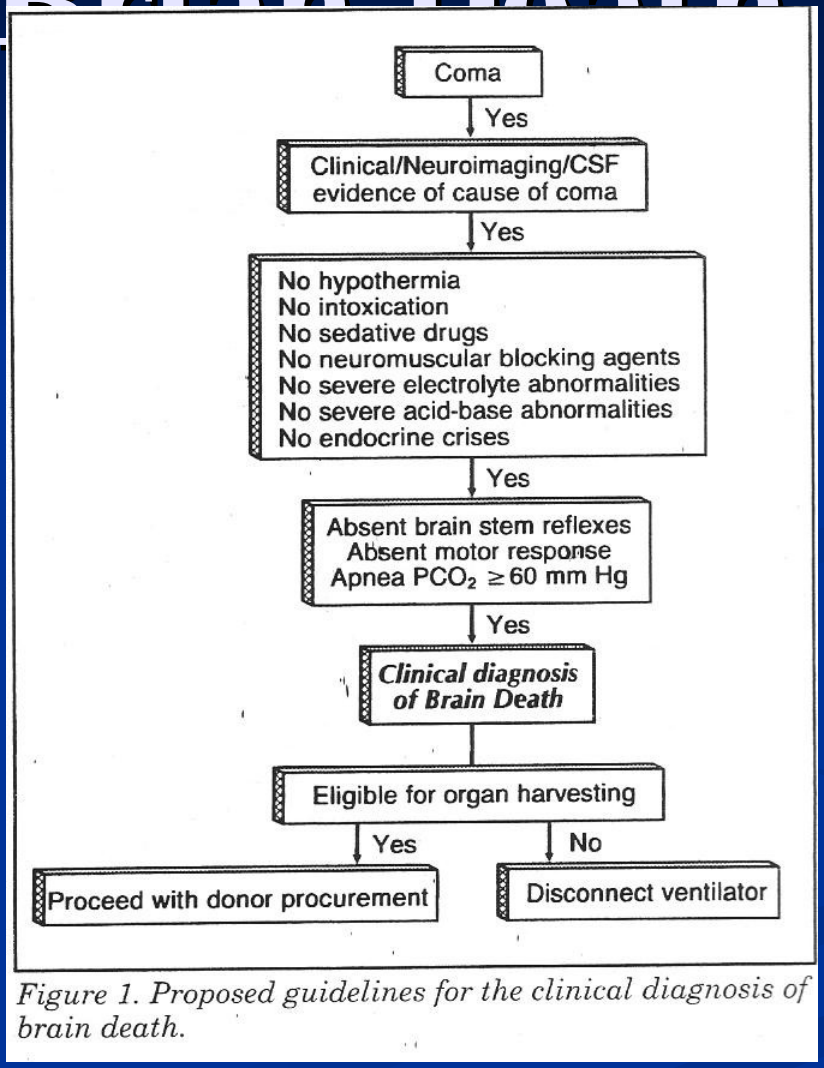


Figure 1. Proposed guidelines for the clinical diagnosis of brain death.

Clinical Diagnosis of Brain Death

- Clinical Prerequisites
  - Etiology of coma should be known
  - Exclusion of reversible causes of coma
- Clinical neurologic examination
  - Documentation of coma or unresponsiveness
  - Absence of brain stem reflexes
  - Apnea when $PaCO_2 > 60mmHg$ or 20mmHg over baseline value.

Prerequisites to the Diagnosis

Evidence of acute CNS catastrophe

compatible with brain death.

- Clinical or Neuroimaging

Exclusion of reversible medical conditions that can

confuse the clinical assessment

- Severe electrolyte, acid base and endocrine disturbance
- Absence of drug intoxication and poisoning
- Absence of sedation and neuromuscular blockade
- Hypotension (suppresses EEG activity and CBF)
- Absence of severe hypothermia (core temp < 32 C)

Confirmation of Coma

- May proceed with confirmation of coma once prerequisites have been met. (etiology and reversibility).
- Document presence or absence of cerebral motor response to a standardized painful stimulus.
  - Supraorbital pressure.
  - Tempromandibular joint.
  - Nail-bed of a finger.

Testing of Brain Stem Reflexes

- May proceed once absence of motor response to painful stimulus has been documented.
- Requires measurement of reflex pathways in the mesencephalon, pons and medulla oblongata.
- Reflexes are lost in a rostal to caudal direction
- The medulla oblongata is the last part of the brain stem to cease function and houses the respiratory nuclei.

Testing of Brain Stem Reflexes

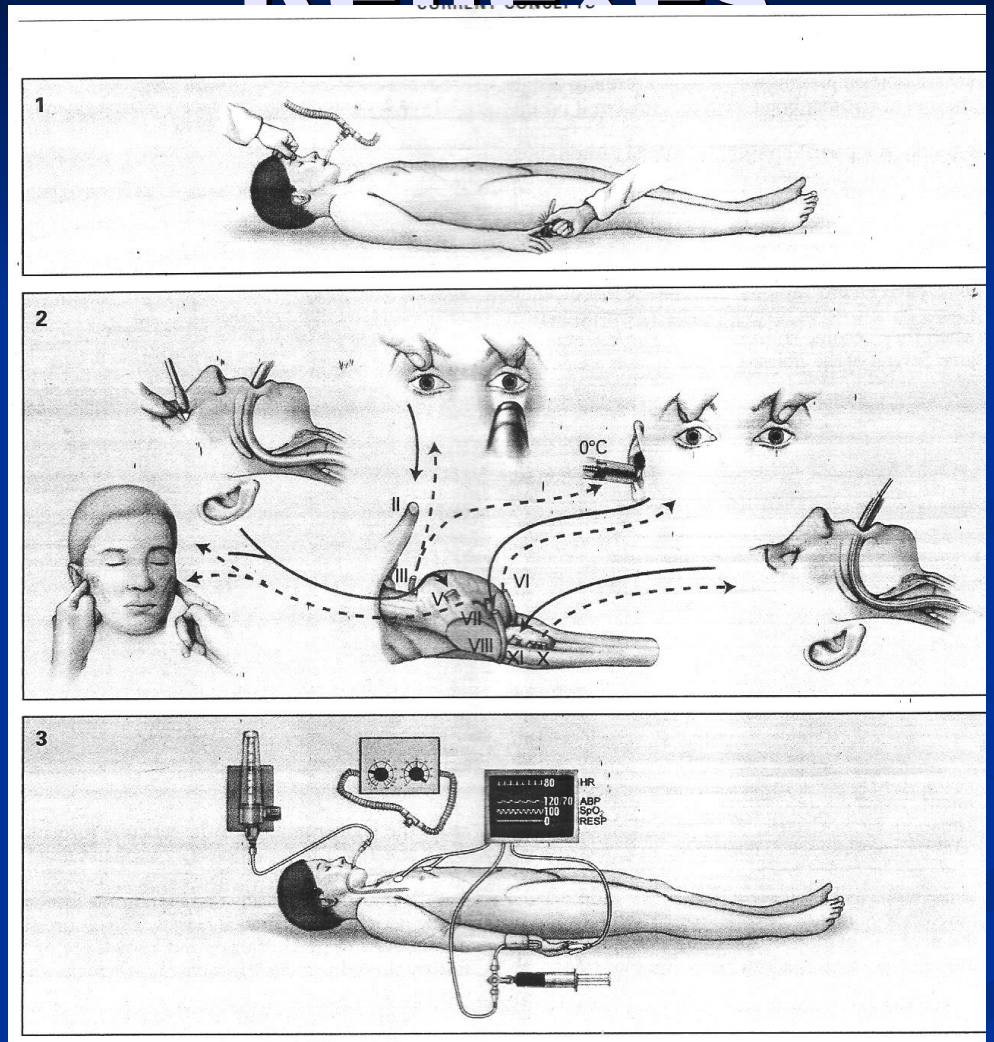


Figure 1. The Steps in a Clinical Examination to Assess Brain Death.

Testing of Brain Stem Reflexes

- **Cranial nerve examination**:

- No pupillary response to light. Pupils midline and dilated 4-6mm.
- No oculocephalic reflex (Doll's eyes) – contraindicated in C- spine injury.
- No oculovestibular reflex (tonic deviation of eyes toward cold stimulus) – contraindicated in ear trauma.
- Absence of corneal reflexes
- Absence of gag reflex and cough to tracheal suction.

Apnea Testing

- Once coma and absence of brain stem reflexes has been confirmed → **Apnea testing**.
- Verifies loss of most rostral brain stem function
- Confirmed by **PaCO2 > 60mmHg** or **PaCO2 > 20mmHg over baseline value.**
- Testing can be associated with hypotension, severe cardiac arrhythmias and elevated ICP.
- Therefore, apnea testing is performed last in the clinical assessment of brain death.
- Consider **confirmatory tests** if apnea test inconclusive.

Apnea Testing

- Following conditions **must** be met before apnea test can be performed:
- Core temp > 36.5 C (97 F).
- Systolic blood pressure > 90mmHg.
- Euvolemia
- Corrected diabetes insipitus
- Normal PaCO2 (PaCO2 > 40mmHg).
- Preoxygenation (PaO2 > 200mmHg).

Procedure for Apnea Testing

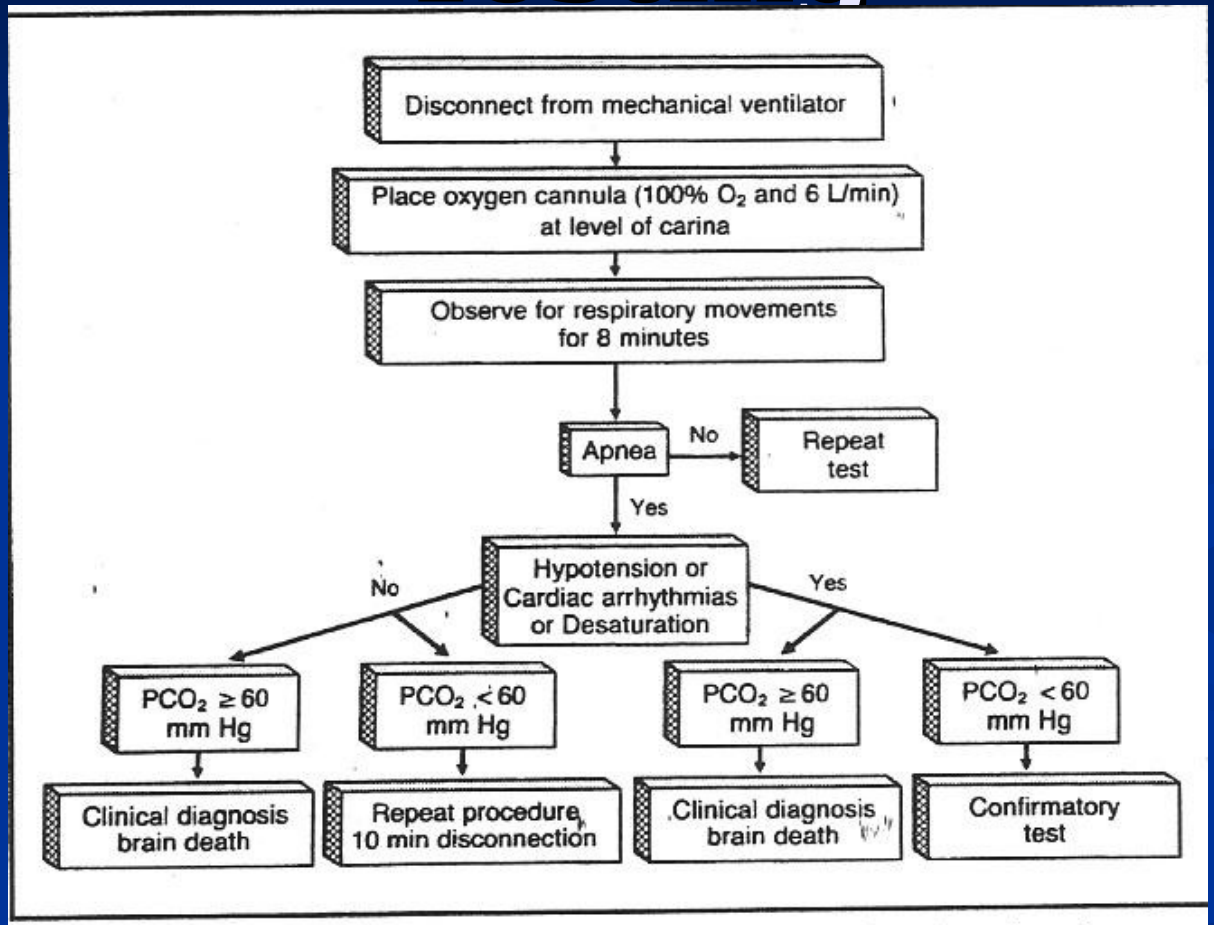


Figure 3. Procedure for the apnea test in brain death.

Confirmatory Testing

- Purely optional when the clinical criteria are met unambiguously.
- “A confirmatory test is needed for patients in whom specific components of clinical testing cannot be reliably evaluated”
  - Coma of undetermined origin
  - Incomplete brain stem reflex testing
  - Incomplete apnea testing
  - Toxic drug levels
  - Children younger than 1 year old.
  - Required by institutional policy

Confirmatory Tests

Choice of testing is left to the discretion of the

attending physician or transplant center.

- Radioactive Isotope Angiography (T-99)
- Transcranial Doppler Ultrasonography
- Conventional Cerebral Angiography
- Electroencephalography
- Somatosensory evoked potential

Brain Death in Children

- Clinical exam is same as in adults.
- Testing criteria depends on age of child.

  - Neonate < 7 days → Brain death testing is not valid.
  - 7 days – 2 months
  - Two clinical exams and two EEG 48 hrs apart.
  - 2 months – 1 year
  - Two clinical exams and two EEG 24 hrs apart.
  - or two clinical exams, EEG and blood flow study.
  - Age > 1 year to 18 years
  - Two clinical exams 12 hrs apart, confirmatory study *optional*

Declaration of Brain Death

- Etiology of the cause of coma.
- Exclusion of reversible causes of coma.
- Clinical confirmation of coma.
- Confirmation of absence of brain stem reflexes to include absence of spontaneous respiration.
- Repeat clinical exam 6 hrs following initial exam confirms irreversibility.
- Confirmatory testing if applicable.

Etiology of Brain Death

- Severe head trauma
- Aneurismal subarachnoid hemorrhage
- Cerebrovascular injury
- Hypoxic-ischemic encephalopathy
- Fulminant hepatic necrosis
- Prolonged cardiac resuscitation or asphyxia
- Tumors

Pathophysiology

- Causes of brain death ultimately produce edema
- **Vasogenic edema** – Induced by an increase in cerebrovascular permeability after leaking of serum proteins into brain parenchyma.
- **Cytotoxic brain edema** – Occurs in hypoxia and ischemic conditions. Result is failure of energy dependent cell membrane pumps. Loss of osmoregulation increases entry of water into the brain parenchymia.

Pathophysiology

- Progressive mass effect leads to worsening ICP, venous engorgement and cerebral ischemia.
- Brain stem herniates through foramen magnum further compromising cerebral and brain stem blood flow.
- Leads to brain stem ischemia and infarction followed by complete cessation of intracranial circulation.
- Absence of IBF > 10 min is incompatible with intact brain function.
- Total brain infarction results in aseptic necrosis.
- Within 3-5 days the brain becomes a liquefied mass “respirator brain”.

Pathophysiology

- Loss of **brain stem function** results in systemic physiologic instability:
- Loss of vasomotor control leads to a hyperdynamic state.
- Cardiac arrhythmias
- Loss of respiratory function
- Loss of temperature regulation → Hypothermia
- Hormonal imbalance → DI, hypothyroidism

Pathophysiolgy

Brain death follows an orderly rostrocaudal pattern: cerebrum → pons → medulla → spinal cord.

- **Cerebrum**
- Infarction results in destruction of hypothalamic and pituitary structures.
  - Hypothermia (loss of temperature regulation)
  - Loss of endocrine regulation
- **Pontine ischemia**
- Occurs with elevated ICP or brainstem herniation.
- *Cushing's response,* mixed vagal & sympathetic outflow (bradycardia, HTN, irregular breathing)

Pathophysiology

- **Medullary ischemia**

- *Sympathetic or Autonomic Storm*.
  - Occurs early in brain stem death.
  - Ischemia to vagal & cardio-motor nuclei results in unopposed catecholamine surge.
  - Causes intense systemic and coronary artery vasoconstriction, tachycardia and elevated ICP.
  - Blood volume shifts to capacitance vessels.
  - Hyper-sympathetic state can lead to systemic organ and tissue ischemia.

Medullary Ischemia (cont)

- *Myocardial injury* is dependant of intensity of catecholamine surge.
  - Myocytolysis and necrosis
  - Conduction tissue necrosis
  - Subendocardial necrosis
  - Cellular edema secondary to increased intracellular calcium
  - EKG abnormalities & dysrrhythmias

Medullary Ischemia (cont)

- *Pulmonary injury*

- Varying degrees of sympathetic storm can lead to **pulmonary congestion**
- Elevated SVR and PVR results in increased pulmonary capillary bed pressure and endothelial damage.

- **Lower Medulla**

- Ischemia to respiratory center results in apnea.

Pathophysiology

- **Complete brain stem ischemia**
- Results in a progressive loss of spinal sympathetic pathways & total sympathetic denervation.
- Global loss of sympathetic vascular tone & profound reduction in SVR leads to cardiovascular collapse and end organ ischemia.
- The pituitary and hypothalamic regulatory system may also become affected as ischemia spreads leading to the loss of many homeostatic control mechanisms.

US System of Organ Procurement & Transplantation

- 1900's Dr. Alexis Carrel received Nobel prize for pioneering microsurgical techniques for vascular organ transplantation.
- 1954 Peter Bent Brigham Hospital, Boston. First successful kidney transplant from a living identical twin donor.
- 1962 Brigham & Woman's Hospital, Boston. The first use of immunosuppressive drugs to control rejection in a cadaveric kidney recipient.

US System of Organ Procurement & Transplantation

- **1968 – Uniform Anatomical Gift Act**
  - Enactment of Uniform Donor Card.
  - Allows for family consent for organ donation on deceased behalf.
- Throughout the 1960's continued advances in microvascular surgery and medicine brought the science of transplantation into the realm of accepted treatment for end-stage organ disease.
- By the early 1980's there was a recognized need for a formalized system to oversee the distribution of organs in an equitable fashion.

National Organ Transplant Act

- **1984 Task force on Organ Procurement and Transplantation**

- Concluded that an overwhelming gap existed between the demand for organs and available supply.
- Recommended that all states develop legislation to provide for the diagnosis of death based on neurologic criteria.
- Required implementation of organ request legislation in all states.
- Provided framework for a national Organ Procurement and Transplantation Network (OPTN) to facilitate organ recovery and placement

National Organ Transplant Act

- **1986 – United Network of Organ Sharing (www.unos.org)**

- Awarded the contract to serve as the coordinating network (OPTN) for organ procurement and transplantation.
- Grants approval & regulates activities of transplant centers and organ procurement organizations.
- Establishes policy for the assurance of quality organ procurement and the equitable distribution of organs.
- Acts as the coordinating agency between the OPO's and the transplant centers.
- OPTN maintains the national transplant database and waiting list of all candidates awaiting cadeveric organ transplantation.

Organ Procurement Organizations

- 60+ **OPOs** exist across the United States.
- Each is federally designated by the department of HHS for a specific geographical region.
- **Washington Regional Transplant Consortium.** Responsible for the regional organ and tissue donation, recovery and allocation process.
- 1986 Federal law requires all hospitals to be affiliated with an organ procurement organization.
- 1987 congressional legislation required all transplant centers & OPO's to be members of the OPTN to receive funding through Medicare or Medicaid.

U.S. Organ Transplant Waiting List

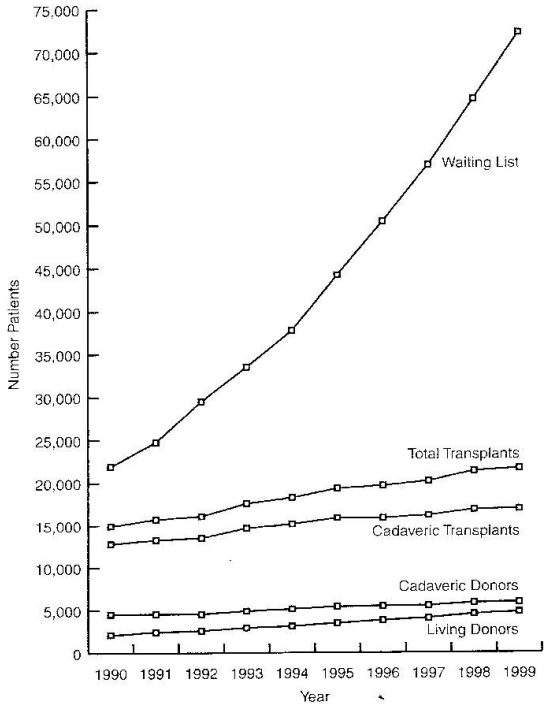
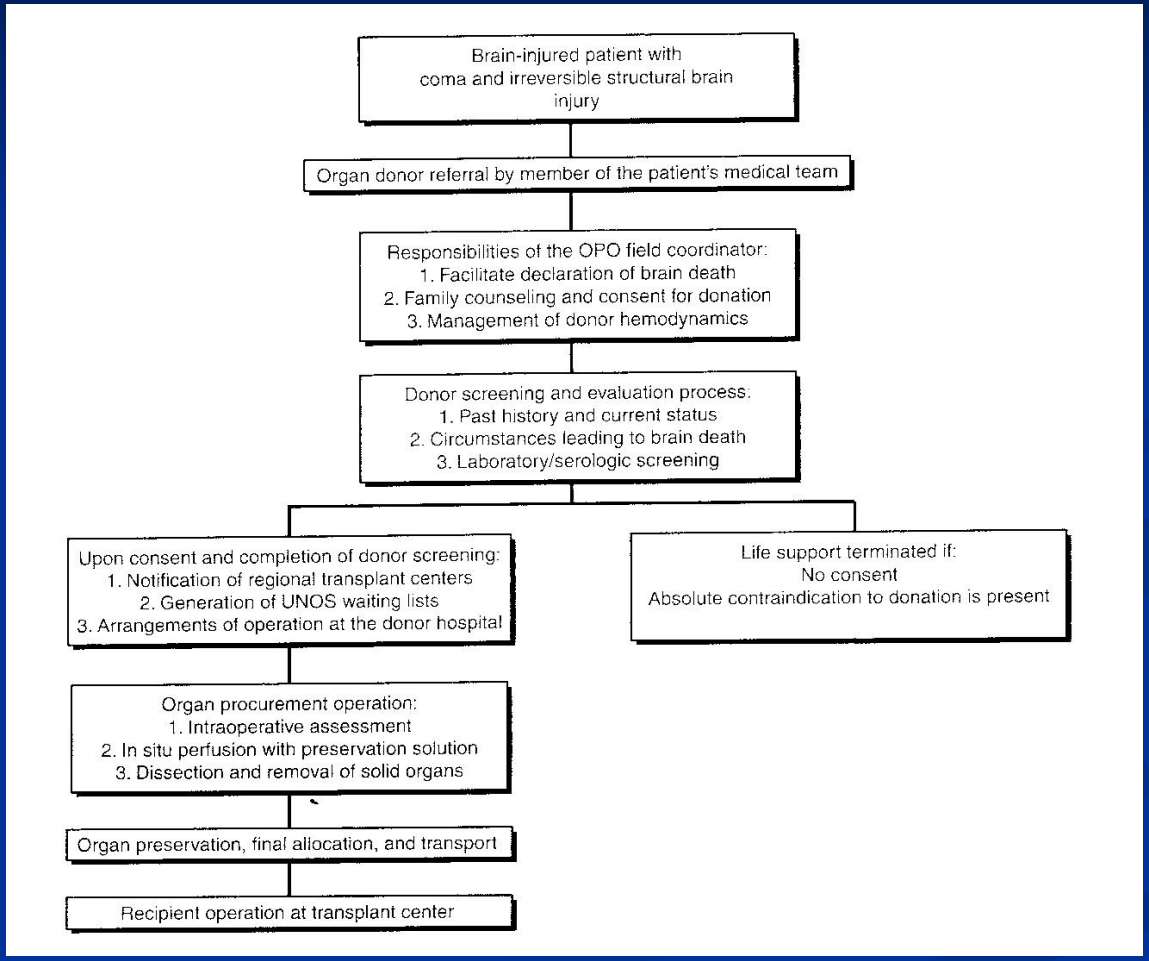


Figure 51–1. Total patients on U.S. organ transplant waiting lists, total transplants performed, and total donors procured from 1990 to the end of 1999. *(Data from the 2000 Annual Report of the U.S. Scientific Registry for Transplant recipients and the Organ Procurement and Transplantation Network: http://www.unos.org/Data/anrpt00/ar00_table08_01_all.htm and http://www.unos.org/Data/anrpt/r_data_fig_01.htm. Accessed January 6, 2002).*

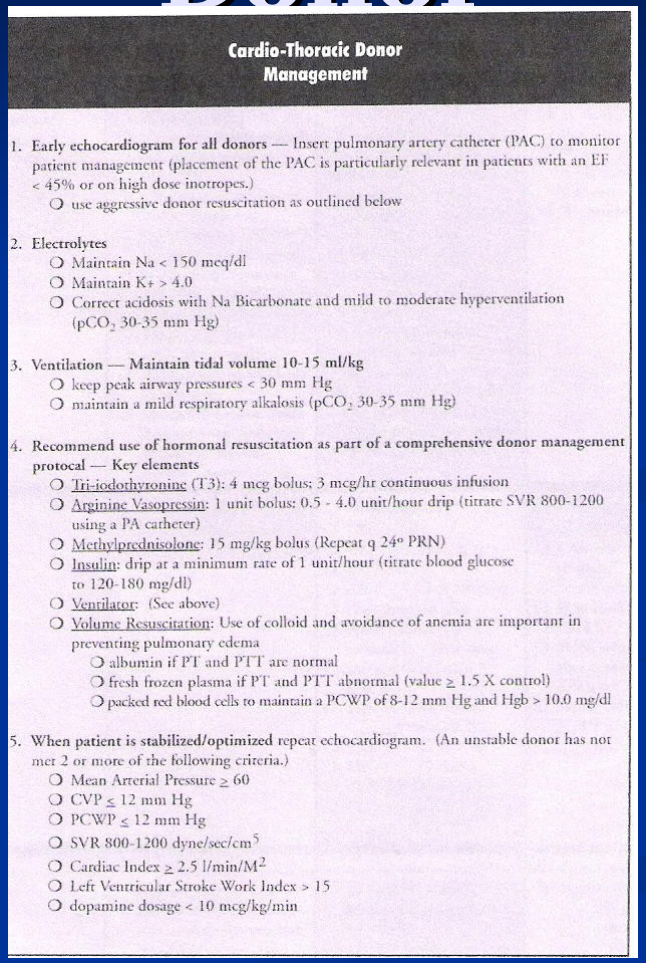
Overview of the Organ Donation Process



Perioperative Management

- **Following the diagnosis of Brian Death**
- Therapy shifts in emphasis from cerebral resuscitation to optimizing organ function for subsequent transplantation.
- The normal sequelae of brain death results in cardiovascular instability & poor organ perfusion.
  - Providing hemodynamic stabilization.
  - Support of body homeostasis.
  - Maintenance of adequate cellular oxygenation and donor organ perfusion.
- Without appropriate intervention brain death is followed by severe injury to most other organ systems. Circulatory collapse will usually occur within 48hrs.
- UNOS Critical Pathway for the Organ Donor.

UNOS
Critical Pathway for the Organ Donor



Cardio-Thoracic Donor Management

1. **Early echocardiogram for all donors** — Insert pulmonary artery catheter (PAC) to monitor patient management (placement of the PAC is particularly relevant in patients with an EF < 45% or on high dose inotropes.)
   - ❍ use aggressive donor resuscitation as outlined below

2. Electrolytes
   - ❍ Maintain Na < 150 meq/dl
   - ❍ Maintain K+ > 4.0
   - ❍ Correct acidosis with Na Bicarbonate and mild to moderate hyperventilation (pCO_2 30-35 mm Hg)

3. Ventilation — **Maintain tidal volume 10-15 ml/kg**
   - ❍ keep peak airway pressures < 30 mm Hg
   - ❍ maintain a mild respiratory alkalosis (pCO_2 30-35 mm Hg)

4. **Recommend use of hormonal resuscitation as part of a comprehensive donor management protocol** — Key elements
   - ❍ Tri-iodothyronine (T3): 4 mcg bolus; 3 mcg/hr continuous infusion
   - ❍ Arginine Vasopressin: 1 unit bolus; 0.5 - 4.0 unit/hour drip (titrate SVR 800-1200 using a PA catheter)
   - ❍ Methylprednisolone: 15 mg/kg bolus (Repeat q 24° PRN)
   - ❍ Insulin: drip at a minimum rate of 1 unit/hour (titrate blood glucose to 120-180 mg/dl)
   - ❍ Ventilator: (See above)
   - ❍ Volume Resuscitation: Use of colloid and avoidance of anemia are important in preventing pulmonary edema
     - ❍ albumin if PT and PTT are normal
     - ❍ fresh frozen plasma if PT and PTT abnormal (value ≥ 1.5 X control)
     - ❍ packed red blood cells to maintain a PCWP of 8-12 mm Hg and Hgb > 10.0 mg/dl

5. When **patient is stabilized/optimized** repeat echocardiogram. (An unstable donor has not met 2 or more of the following criteria.)
   - ❍ Mean Arterial Pressure ≥ 60
   - ❍ CVP ≤ 12 mm Hg
   - ❍ PCWP ≤ 12 mm Hg
   - ❍ SVR 800-1200 dyne/sec/cm^5
   - ❍ Cardiac Index ≥ 2.5 l/min/M^2
   - ❍ Left Ventricular Stroke Work Index > 15
   - ❍ dopamine dosage < 10 mcg/kg/min

Perioperative Management

- Incidence of pathophysiologic changes following brain stem death.
  - Hypotension 81%
  - Diabetes Insipidus 65%
  - DIC 28%
  - Cardiac arrhythmias 25%
  - Pulmonary edema 18%
  - Metabolic acidosis 11%

Physiologic changes During Brain Stem Death – Lessons for Management of the
Organ Donor. The Journal of Heart & Lung Transplantation Sept 2004 (suppl)

Cardiovascular System

- Hypotension and hemodynamic instability
- **Neurogenic shock**
  - Result of defective vasomotor control and subsequent loss

  progressive loss of SVR..
- **Hypovolemic shock**
  - Therapeutic dehydration for cerebral edema.
  - Hemorrhage.
  - Diabetes insipidus with massive diuresis.
  - Osmotic diuresis due to hyperglycemia.
- **Cardiogenic component**
  - Hypothemic depression of myocardial contractility.
  - Left ventricular dysfunction

Cardiovascular System

- **Intensive care management**
- "Rules of 100's"
  - Maintain SBP > 100mmHG
  - HR < 100 BPM
  - UOP > 100ml/hr
  - PaO2 > 100mmHg
- Aggressive fluid resuscitative therapy directed at restoring and maintaining intravascular volume. SBP > 90mmHg (MAP > 60mmHg) or CVP < 12mmHg.
- Early use of colloid are important in preventing pulmonary edema.
- Albumin if PT and PTT are normal
- FFP if PT and PTT abnormal (value > 1.5 X control)
- PRBC to maintain a PCWP of 8-12mmHg and Hgb > 10 mg/dl

Cardiovascular System

- Dextran 40 – used by some centers to improve microcirculation, tissue oxygenation and reduce risk of thromboembolic complications.
- Persistent hypotension despite adequate filling pressures require pharmacologic support as directed by the OPO coordinator.
- Vasopressin → First line agent
  - Independently improves SVR.
  - Reduces need for exogenous inotropic support.
  - Treatment of diabetes insipidus.

Pennefather SH, Bullock RE, et al. **Use of low dose arginine vasopressin to support brain-dead organ donors.** Transplantation 1995; 59: 58-62.

Respiratory System

- Goals are to maintain health of lungs for transplant while optimizing oxygen delivery to other transplantable organs.
- Avoid overhydration.
- Frequent pulmonary toilet.
- Ventilatory strategies aimed to protect the lung.
- Avoid oxygen toxicity by limiting Fi02 to achieve a Pa02 100mmHg & PIP < 30mmHg.

Endocrine System

- Brain death may interrupt hypothalamic-pituitary axis leading to serum hormone depletion.
- Consequent hypothyroidism & adrenal insufficiency may lead to depletion of the mitochondrial ability to regenerate ATP resulting in functional organ instability

Novitsky D, Cooper DKC, Morrel D et al. **Changes from Aerobic to Anaerobic metabolism after Brain Death, and Reversal following T3 Therapy.**
TRANSPLANT 1988; 45: 32-36.

Endocrine System

- Current guidelines recommend the use of a standardized hormonal resuscitation package.
  - Methylprednisolone 15mg/kg bolus
  - Triiodothyronine (T3) 4mcg bolus, 3mcg/hr.
  - Arginine vasopressin 1 unit bolus, 0.5-4 units/hr (titrate SVR 800 – 1200)
- Goal: treatment of potential cardiac arrhythmias, diabetes insipidus, hypotension, metabolic acidosis .

Rosendale JD, Kauffman HM, et al. **Aggressive pharmacologic Donor Management Results in More Transplanted Organs.** TRANSPLANTATION 2003: 75: 482

Effects of Endocrine Dysfunction

- **Central Diabetes Insipidus**
- Early depletion of ADH
- Characterized by inappropriate diuresis leading to severe hypovolemia → hemodynamic and electrolyte instability.
- Treatment is aimed at correcting hypovolemia.
- Management includes replacing free water loss with hypotonic saline or dextrose in water and electrolytes as needed.
- Vasopressin 0.5-0.6 units/hr reduces UOP.
- Goal UOP 100-200 ml/hr.
- Severe cases UOP >1000 ml/hr may respond to DDAVP 0.3mcg/kg or vasopressin 0.1 U/min.

Effects of Endocrine Dysfunction

- **Thyroid hormones**

- Rapid decline in free T3 is seen in brain death.
- Result of impaired TSH secretion and peripheral conversion of T4 to T3.
- Lack of T3 results in **anaerobic metabolism & acidosis.**
- Progressive **loss of cardiac contractility** associated with depletion of high-energy phosphates.

Novitsky D, Cooper DKC, Morrel D et al. **Changes from Aerobic to Anaerobic Metabolism After Brain Death, and Reversal Following Triiodothyronine Therapy.** TRANSPLANT 1988; 45: 32-36.

Effects of Endocrine Dysfunction

- **Thyroid hormones** (continued)
- Studies have demonstrated that the use of T3 **improves tissue and organ perfusion** with subsequent **shift** from anaerobic **to aerobic metabolism** due to:

- T3 activates the cellular mitochondria to maintain aerobic respiration with a shift to normalize lactate and free fatty acid metabolism.
- Increased arterial blood pressure.
- Increased left ventricular SWI and CO.
- Decreased inotrope requirements.

Effects of Endocrine Dysfunction

- **Steroid Replacement**
- Improves donor organ function and graft survival.
- Increases tissue oxygenation and donor lung recovery.
- Improves cardiac function following transplantation.
- Attenuate the effects of proinflammatory cytokines released as a consequence of brain death.

Rosendale JD, Kauffman HM, **Hormonal Resuscitation Yields More Transplanted Hearts, with Improved Early Function.** TRANSPLANT 2003; 75: 1336-1341

Effects of Endocrine Dysfunction

- **Fall in insulin levels**
- Leads to systemic hyperglycemia with severe osmotic diuresis and profound hypovolemia.
- Decreased intracellular glucose concentration.
- Development of a cellular energy deficit
- Conversion to an anaerobic state and metabolic acidosis.
- Management: Insulin infusion 1 unit/hr minimum (titrate blood glucose to 120-180 mg/dl)

Loss of Homeostasis

- **Hypothermia**
- Loss of hypothalamic temperature regulation.
- Fall in metabolic rate.
- Core temps < 32 degrees
  - Dysrrhythmias
  - Bradycardia and myocardial depression
  - Coagulopathy
  - Pancreatitis
  - Left shift in oxyhemoglobin dissociation curve
- **Goal →** Aggressive warming to maintain temp > 34 C.

Other Systems

- **Infection**
- Surveillance for infection, routine blood cultures/cxr.
- Routine administration of nonnephrotoxic antibiotics to prevent transmission of infection to immunosuppressed recipient.
- **DIC**
- Passage of necrotic brain tissue into the circulation may activate the clotting cascade in association with the disruption of endothelial surfaces.
- DIC may persist despite factor replacement necessitating early organ retrieval.

Organ Procurement

- Multi-organ procurement occurs in the operating room environment under sterile technique.
- Anesthesia support is required to provide physiologic support of the donor during the procurement phase.
- Intensive care management continues intraoperatively with an emphasis on optimum organ perfusion and oxygenation.
- Anesthesiologist should verify documentation of family consent for organ donation and certification of death.

Organ Procurement

- Organ harvest is performed through a midline incision from suprasternal notch to pubic symphasis.
- Procurement and in situ core cooling of organs.
- **Surgical Technique "no touch" en bloc procedure**

- Minimize ischemic injury from surgically induced arterial vasospasm.
- Provides for even flushing and cooling of organs.
- Organ preservation is enhanced using cold ischemic preservative solutions. Organs are rapidly flushed & cooled to 4 C slowing
  cellular metabolism and oxygen consumption.

An Improved technique for Multiple Organ Harvesting
University of Pittsburg School of Medicine, Dept. of Surgery
Surgery, Gynecology & Obstetrics Oct 1987 Vol 165

Organ Procurement

- Donor organ preservation (cold ischemic time):
  - Heart & Lungs 3-4 hrs
  - Pancreas 6 hrs
  - Liver 8 hrs
  - Kidneys 36 hrs
- Organ Preservation
  - Use of hyperosmolar preservative solutions suppress cell swelling that is induced by hypothermic storage.
  - Organs are placed in sterile containers and packed in ice in preparation for transport to transplant center.

Intraoperative Management

- **Monitoring**
  - Standard ASA monitors
  - Arterial line, CVP, +/- PA Catheter, Foley
- **Lab**
  - Q 1 hr ABG, Hct, Electrolytes and blood glucose.
- **Use of neuromuscular blocking agents**
  - Used to avoid reflex neuromuscular activity.
  - Facilitates surgical exposure.
  - Avoid histamine releasing agents
- **Ventilator Management**
  - Maintain adequate oxygenation Pa02 75-100 mmHg
  - Avoid oxygen toxicity, Fi02 = 40 mmHg
  - Avoid lung barotrauma PIP < 30mmH
  - Adjust respiratory rate to maintain PaCo2 between 35-45mmHg.

Anesthetic Management

- **Maintaining Hemodynamic Stability**
- Reflex pressor response to nociceptive stimuli
  - Excessive operative blood loss and renal graft ischemia
  - Management consists of afterload reduction using short acting agents. (NTG, SNP or isoflurane)
- Guidelines for maintaining CV homeostasis.
  - Apply rule of 100's
  - CVP 8-12 cm H20, PCWP 10 +/- 3 , PAP 15 +/- 4
  - CO 4-8 l/min, Mixed venous saturation > 75%

Anesthetic Management

- **Maintaining Hemodynamic Stability**
- Initial management involves fluid resuscitation with crystalloid or colloid.
- Continue triple therapy (steroids, T3, vasopressin).
- Insulin infusion may be required.
- Maintain Hct > 30% to facilitate O2 carrying capacity to donor organs.
- Dopamine 2-5 mcg/kg/min.
- Vasopressin is first line agent for severe hypotension.
- Addition of inotropes as indicated and directed by OPO surgeon once adequate filling pressures are achieved with volume resuscitation.

Anesthetic Management

- Anesthetic Record:

  - Proximal aortic x-clamp time & infusion of cardioplegia soln.

- Heparin 20,000 Units (300 u/kg in children)

  - Given after aortic cannulation and prior to infusion of cold

    potassium cardioplegia.

- Anesthetic support ends with occlusion of the proximal aorta and in situ organ flushing.
- At this time all monitoring along with ventilation and supportive measures are discontinued.
- Removal of donor organs begin.